Chapter 12
Green Chemistry Approach Using Heterogeneous Catalysts in the Heterocyclic Synthesis

Sudesh Kumar, Prachi Rathi, K. L. Ameta and Dharma Kishore

Contents

1 Introduction ... 367
2 Synthesis of Heterocyclic Compounds ... 369
3 Catalytic Applications in Heterocyclic Synthesis ... 369
  3.1 Synthesis of Five-Membered Heterocycles ... 369
  3.2 Synthesis of Six-Membered Heterocycles ... 384
References ... 388

Abstract The present chapter deals with the recent developments in green chemistry approach using heterogeneous catalysts in heterocyclic synthesis. The process of heterogeneously catalysed reactions of furan, oxazoline, pyrazole, piperidine, piperazine, pyridine and their derivatives are discussed.

Keywords Biocatalysis · Diastereoselective · Microwave-assisted reaction

1 Introduction

Chemical developments bring new environmental problems and harmful, unexpected side effects [1]. The present economy remains utterly dependent on a massive inward flow of natural resources that include vast amounts of nonrenewable [2] reverse flow of economically spent matter back to the ecosphere [3]. Chemical sustainability problems are determined largely by these economy–ecosphere materials flows [4]. It has become imperative to the development of the technological dimension of a sustainable civilization [5]. In the 1980s and 1990s, several envi-

---

S. Kumar (✉) · P. Rathi · D. Kishore
Department of Chemistry, Banasthali University, Banasthali 304022, Rajasthan, India
e-mail: sudeshneyol@gmail.com

K. L. Ameta
Department of Chemistry, FASC, Mody University of Science and Technology,
Lakshmangarh 332311, Rajasthan, India

K. L. Ameta, A. Dandia (eds.), *Green Chemistry: Synthesis of Bioactive Heterocycles,*
DOI 10.1007/978-81-322-1850-0_12, © Springer India 2014

ronmentally conscious terms entered the chemical arena, e.g. clean chemistry, environmental chemistry, green chemistry, benign chemistry and sustainable chemistry. These terms are not well defined and are subject to a debate among chemists [6–7].

Modern organic synthesis eagerly demands methods that allow the preparation of target-relevant products from simple and readily available precursors in a rapid and economical fashion [8–10]. The use of hazardous catalysts and reagents is one of the most important aspects of eco-friendly chemistry. Reagent chemists are working towards the development of more benign and selective reagents that require ambient conditions. The elimination of hazardous solvents is one of the prime concerns among them. In recent years, microwave-assisted organic synthesis (MAOS) has developed into a popular branch of synthetic organic chemistry [11–12]. One of the most fundamental obstacles in developing technologies is to minimize the energy consumption and to eliminate/minimize the use of hazardous solvents.

Green chemistry provides the design and development of sequential processes that use a set of principles that eliminates or reduces hazardous substances in the manufacture, design and application of chemical products. It is a highly effective approach to pollution prevention [13–14]. Organic compounds that contain heterocyclic moieties are quite significant because of their interesting biological properties [15–16]. Heterocyclic compounds form important building blocks for naturally occurring and biologically active compounds. The application of catalytic methods can have highly efficient catalytic efficiency and substrate generality [17]. Heterocyclic compounds have been extensively studied for their biological applications like antiviral, antibacterial, antifungal, antimalarial [18], antileukemic agents [19], antifertility activity, antitubercular, antipyretic, antitumor and anticancer [20].

Conventional methods of organic synthesis usually need longer heating time and elaborate and tedious procedures which result in higher cost of process, and the excessive use of solvents and reagents leads to environmental pollution [21–22]. Microwave-induced organic reactions have emerged as a new ‘lead’ in organic synthesis [23]. Microwave reactions under solvent-free conditions are attractive in reducing pollution, lowering the cost and offering high yields together with simplicity in processing and handling [24]. The salient features of the microwave approach are shorter reaction times, simple reaction conditions and enhancements in yields [25]. The microwave-enhanced chemical reactions are gaining importance due to the advantages and environmentally friendly processes they offer, as compared to conventional reactions [15].

Organic reactions focus on the number of atoms being transformed during the specific synthetic transformation from one phase to another. The intention of green chemistry is to present an illustrative approach as to how one evaluates a synthesis with regard to its environmental consequences. The precise nature of the specific starting organic material and the by-products has an overriding importance when evaluating the environmental aspects of a given synthetic sequence. The green chemistry approach minimizes the use of cumbersome separation, recrystallization, distillation, chromatography and other techniques which minimize the formation of undesired by-products. Toxicity of organic chemicals has a direct or indirect effect on global environmental problems, i.e. acute lethality, algal blooming, neurotoxicity, ozone depletion, endocrine disruptions and global warming. Wherever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment. Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances. Substances used in a chemical process should be chosen so as to minimize the potential for chemical accidents, including releases, explosions and fires.

Heterocycles are important structural motifs of a wide range of natural substances, compounds of pharmaceutical interest and commodity chemicals. Because of this, a large number of methods have been developed to provide access to almost every type of heterocyclic derivative. In this context, transition metal catalysis has played a remarkable and ever-growing role. Heterocyclic chemistry is no exception to this trend. Transition metal-catalysed reactions have been widely employed in the construction of heterocyclic rings providing increased functional group tolerance, simplified procedures and improved yields.

Six-membered nitrogen-containing heterocycles (e.g., pyridines, piperidines and piperazines) are privileged structures that occupy a central role in bioorganic and medicinal chemistry [26–28]. Consequently, developing efficient regioselective and stereoselective methods to obtain these structures has attracted considerable attention during the past decades. These types of heterocycles have been successfully synthesised by using a range of cycloaddition reactions [29–34]. However, the obtained structural diversity is often limited as a result of the partial access of commercially available starting materials.

2 Synthesis of Heterocyclic Compounds

Compounds classified as heterocyclic probably constitute the largest and the most varied family of organic compounds. Carbocyclic compounds, regardless of structure and functionality, may in principle be converted into a collection of heterocyclic analogues by replacing one or more of the ring carbon atoms with a different element. Even if we restrict our consideration to oxygen, nitrogen and sulphur, the permutations and combinations of such a replacement are numerous.

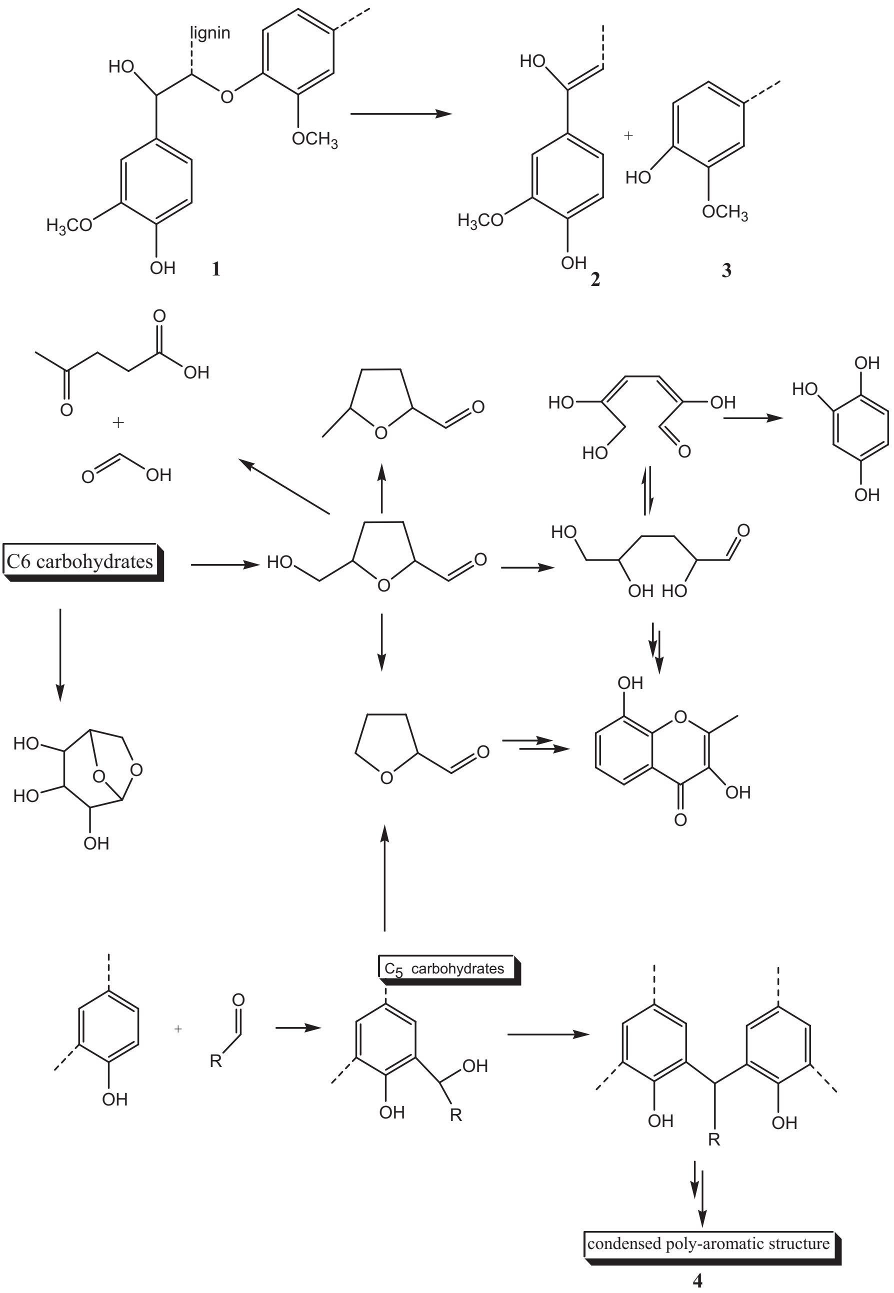
3 Catalytic Applications in Heterocyclic Synthesis

Biological activities of heterocyclic compounds play a crucial role in human life. The aim of this chapter is to design new, safer and environmentally benign methods for the synthesis of heterocyclic compounds for biological applications. All procedures were carried out considering green chemistry principles such as reducing waste generation, increasing atom economy, etc. In all attempts, commercially available and inexpensive starting materials, catalysts and reagents were used in order to make the processes more cost effective.

3.1 Synthesis of Five-Membered Heterocycles

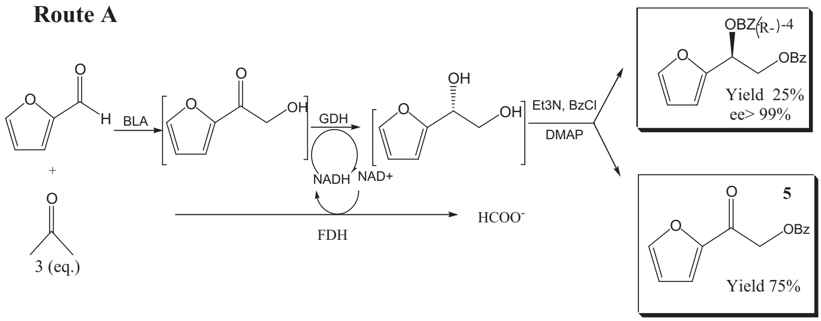
3.1.1 Furan

Formation of an aromatic ring: Reported pathways of decomposition of major wood components and the formation of new functional groups and condensed aromatic units during the torrefaction [35–45] (Scheme 12.1).

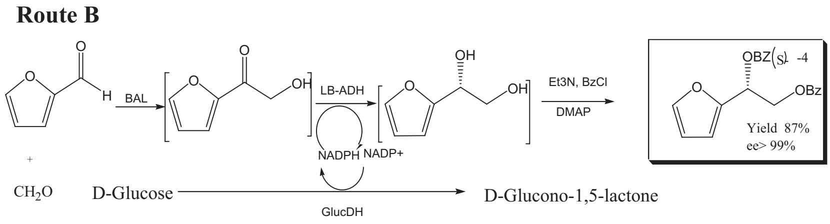

lignin
HO
O
OCH_3
H_3CO
OH
1
2
3
C6 carbohydrates
C_5 carbohydrates
R
condensed poly-aromatic structure
4

Scheme 12.1

Biocatalyzed formation of chiral furane diols: Sufficient amount of **5** as an intermediate despite the higher amount of GDH applied via route **A**, the bottleneck was supposed to be at low activity of GDH towards furan compounds. In fact, in route **B** when *Lb*ADH was applied, with glucose dehydrogenase (GlucDH) for cofactor regeneration, this resulted in excellent isolated yields (87%) and enantioselectivity (>99% ee, (*S*)) [46–49] (Scheme 12.2).



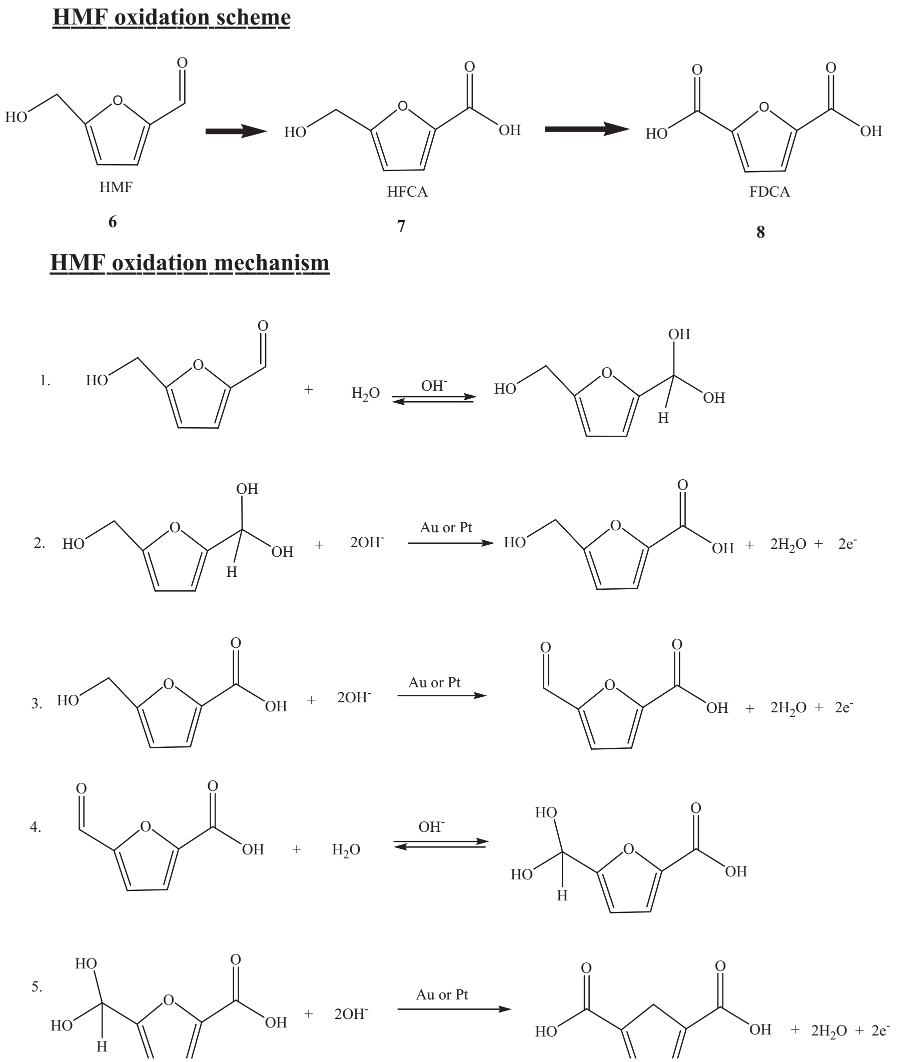
Biocatalytic formation of chiral furane-diols via route A. 40 mL phosphate buffer 50 mmol L-1, pH 8.0, 5% v/v 2-MeTHF, 1.6 mmol furaldehyde, 4.8 mmol formaldehyde, 2.5mmol L-1 MgSO4, 0.15 mmol L-1 ThDP, 168 U BAL, 1500 U GDH, 95 U FDH, NADH/NAD+ 1 mmol L-1 each



Biocatalytic formation of chiral furan-diols. 40 mL phosphate buffer 50 mM, pH 8.0, 5% v/v 2-MeTHF, 1.6 mmol furaldehyde, 3.6 mmol glucose, 4.4 mmol CaCO3, 4.8 mmol formaldehyde, 2.5 mmol L-1 MgSO4, 0.15 mmol L-1 ThDP, 168 U BAL, 50 U Lb-ADH, 2800 U GlucDH, 0.5 mmol L-1 NADPH

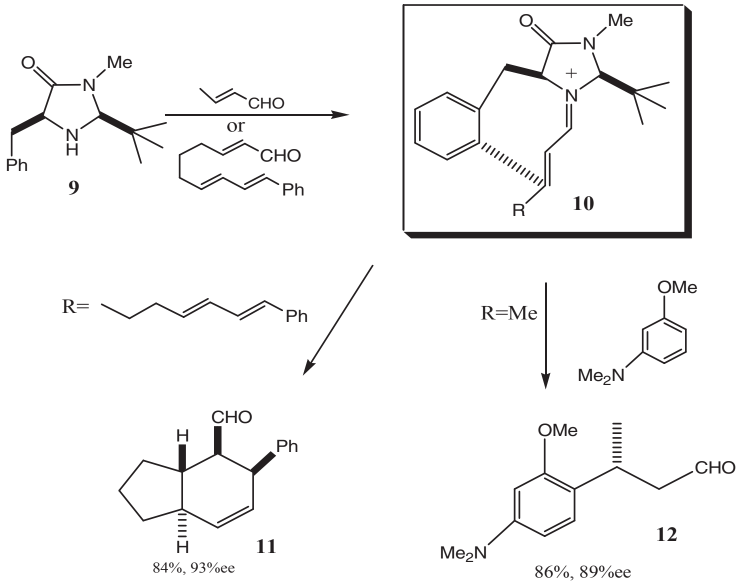
Scheme 12.2

HMF oxidation reaction and mechanism: Hydroxymethylfurfural (HMF) oxidizes in the presence of a base (OH−) and a catalyst, either Pt or Au into HFCA, which on oxidation gives FDCA [50–53] (Scheme 12.3).



Scheme 12.3

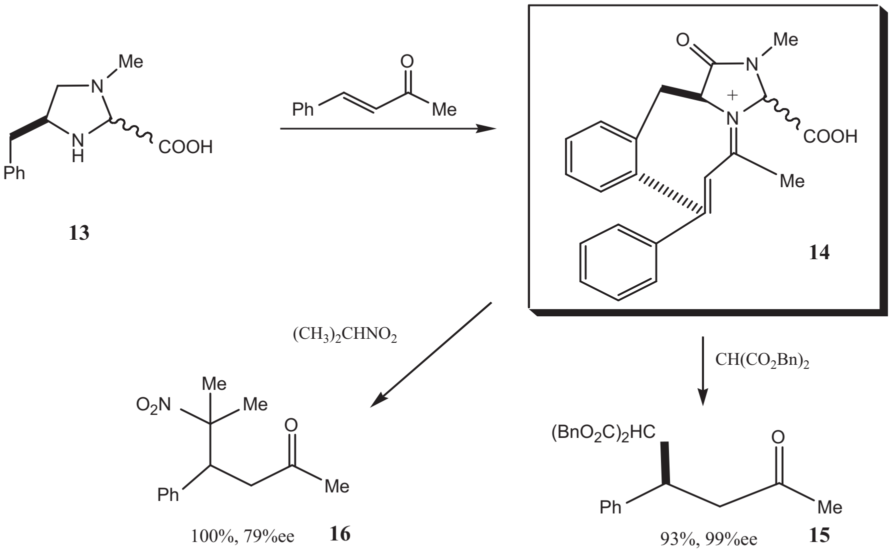
Iminium–π interactions reaction: The enantioselective organocatalytic 1,4-addition reaction of an electron-rich benzene to an α, β-unsaturated aldehyde and an intramolecular Diels–Alder reaction of a trienal has been reported to take place through the sequence of reactions shown in Scheme 12.4. The first step of this reaction is the formation of the intermediary iminium ion **10** from reaction of the catalyst **9** with α, β-unsaturated aldehydes, followed by face-selective addition of the electron-rich benzene derivative to the iminium ion. The subsequent intramolecular Diels–Alder reaction proceeds to give a bicyclic aldehyde **11** bearing four stereogenic centres in 84 % yield and 93 % ee [54–64] (Scheme 12.4).



Enantioselective organocatalytic 1,4-addition reaction to an α,β-unsaturated aldehyde and an intermolecular Diels–Alder reaction.

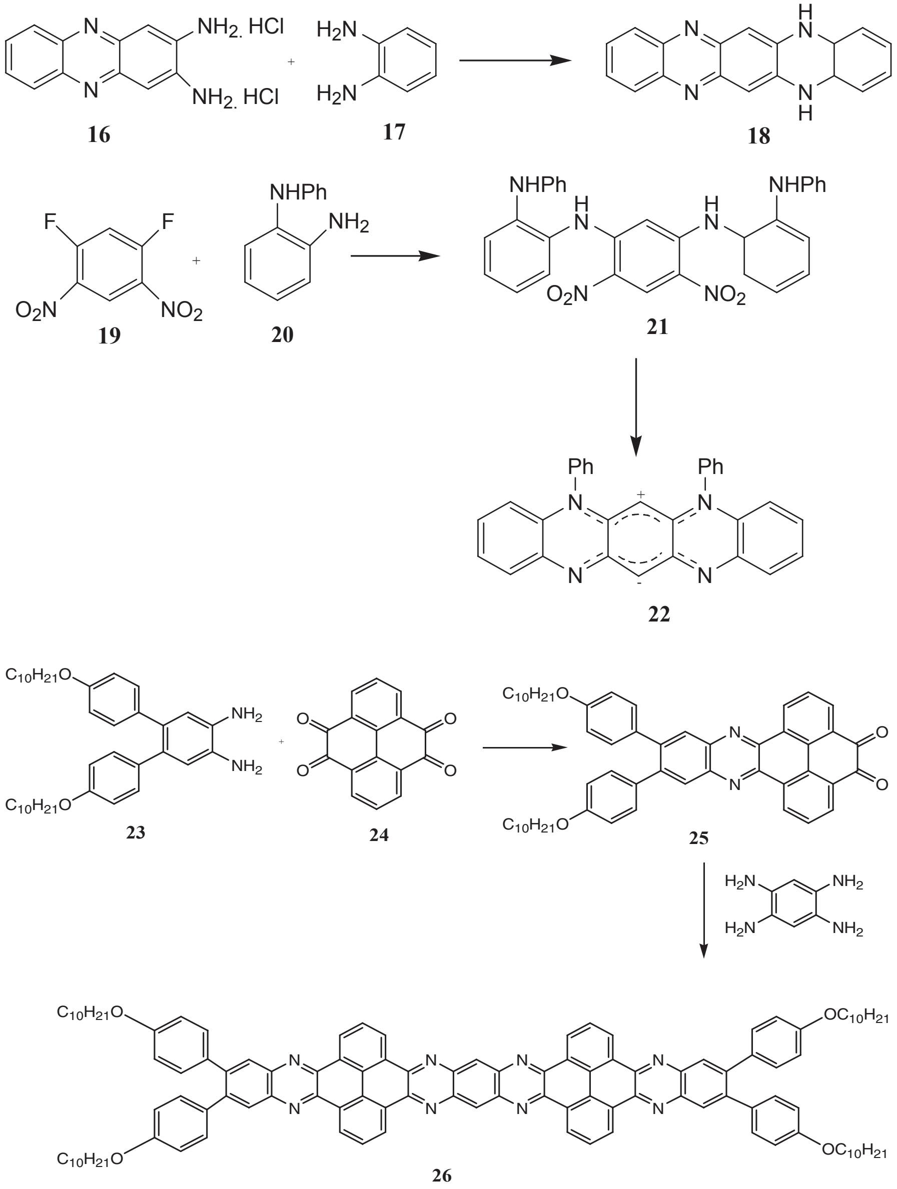
Scheme 12.4

Formation of enones: Jørgensen reported conjugate additions of nitroalkanes and malonates to α, β-unsaturated enones using amine catalyst **13** to give the corresponding adducts **14** with good stereoselectivities [65–67] (Scheme 12.5).



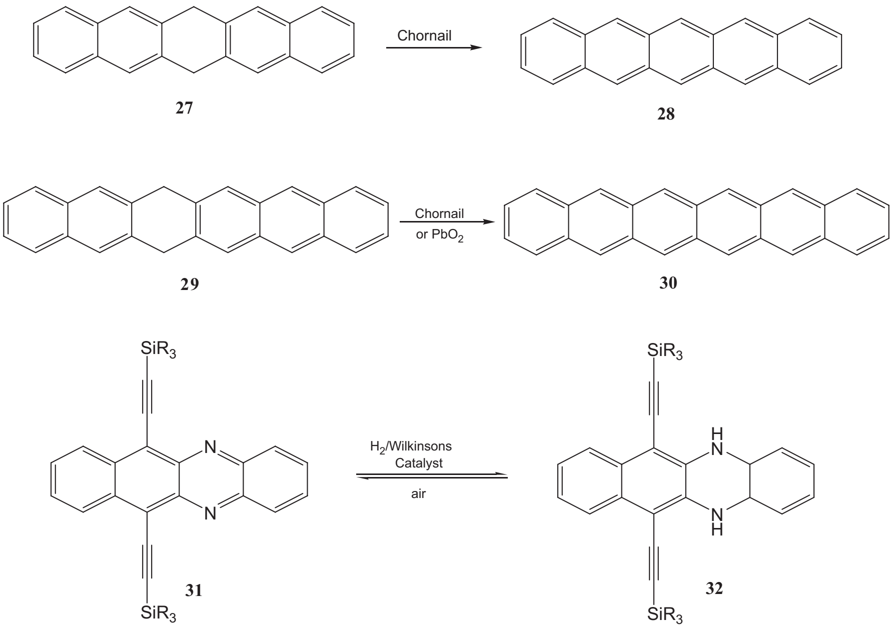
Scheme 12.5

Synthesis of pyrazinacenes: Hepp and Fischer first prepared 5,14-dihydro-5,7,12,14-tetraazapentacene **18** by direct condensation of 2,3-diaminophenazine hydrochloride **16** with *o*-Phenylenediamine **17**. Wudl and co-workers developed a strategy for the synthesis of *syn*-substituted zwitterionic tetraazapentacenes. The preparation involved a double nucleophilic aromatic substitution of 1,5-difluoro-2,4-dinitrobenzene **19** with N-substituted-1,2-phenylenediamines **20** to give 2,4-dinitrobenzene-1,5-diamines **21** in good yield. Hydrogenation of compounds **21** followed by heating in ethanol in air gave the zwitterionic tetraazapentacenes **22**. Pyrazinacenes based on the pyrene moiety have also been prepared. Wang and co-workers developed a series of molecular ribbons with up to linearly fused aromatic rings. Phenylenediamine **23** was condensed with pyrene-4,5,9,10-tetrone **24** to give **25**. A double condensation reaction between benzene tetramine and **25** gave **26** containing linearly fused rings [68–71] (Scheme 12.6).


NH2. HCl
NH2. HCl
16
H2N
H2N
17
18
F
F
O2N
NO2
19
NHPh
NH2
20
NHPh
NHPh
O2N
NO2
21
Ph
Ph
22
C10H21O
C10H21O
NH2
NH2
23
24
25
H2N
NH2
H2N
NH2
OC10H21
OC10H21
26

Scheme 12.6

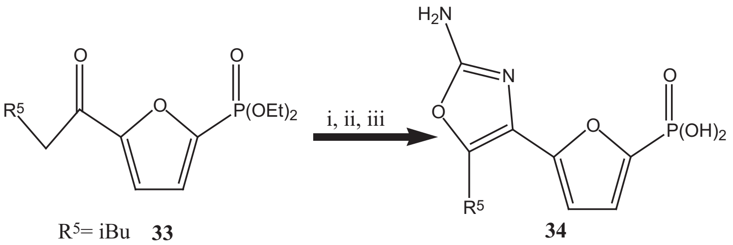
Synthesis of aromatic/antiaromatic compounds: 6,13-Dihydro-6,13-diazapentacene **27** can be oxidized to the fully aromatic form **28** using *p*-Chloranil. As the length of the pyrazinacene is increased, the fully oxidized form becomes even less favoured; for example, the reduced dihydrodiazahexacene **29** cannot be oxidized either with *p*-Chloranil or with lead (IV) oxide. Also, as the number of fused pyrazine rings increases, the reduced form is increasingly favoured. The somewhat unusual stability of the antiaromatic compounds compared to their fully aromatic counterparts was investigated using computational techniques by Bunz and Schleyer. They synthesised two dialkynylated diazatetracenes (**31**, **32**), which could be reversibly reduced/oxidized between the antiaromatic and aromatic forms [72–76] (Scheme 12.7).



Scheme 12.7

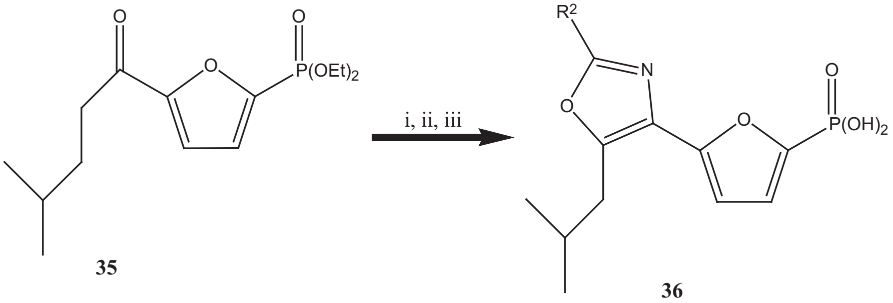
3.1.2 Oxazoles

Synthesis of 2-amino oxazole analogues (Method I): α-Bromination of ketones **33** using copper (II) bromide followed by the treatment with excess urea in *tert*-butanol, and finally trimethylsilyl bromide (TMSBr)-mediated removal of the phosphonate diethyl ester produced oxazole phosphonic acids 34 [77] (Scheme 12.8).



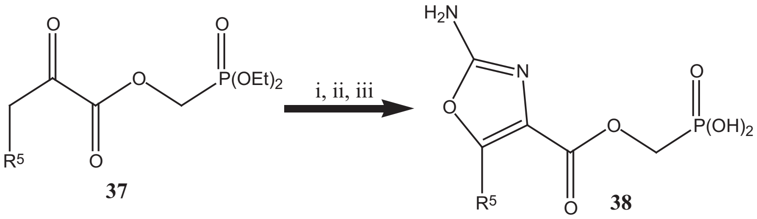
Reagents and conditions: i. $CuBr_2$, EtOAc-$CHCl_3$; ii. Urea, tBuOH, 80°C; iii. TMSBr, CH_2Cl_2.

(Method II): α Bromination of ketones **35** using copper (II) bromide and cyclisation of the resulting bromide with excess R_2CONH_2 in *tert*-butanol followed by TMSBr-mediated removal of the diethyl ester gave oxazoles **36** [77].



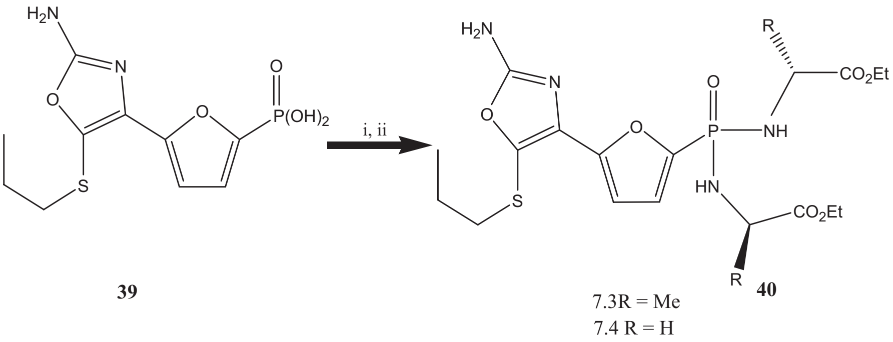
Reagents and conditions: i. $CuBr_2$, EtOAc-$CHCl_3$; ii. Urea, tBuOH, 80 °C; iii. TMSBr, CH_2Cl_2.

(Method III): Oxazoles with ester-linked phosphonic acids **38** that were prepared from pyruvate esters **37**, which were obtained via Fischer esterification as previously reported, were brominated using copper (II) bromide and subsequently cyclised with urea followed by TMSBr-mediated deprotection of phosphonate diester gave oxazoles **38** [77].



Reagents and conditions: i. $CuBr_2$, EtOAc-$CHCl_3$; ii. Urea, tBuOH, 80 °C; iii. TMSBr, CH_2Cl_2

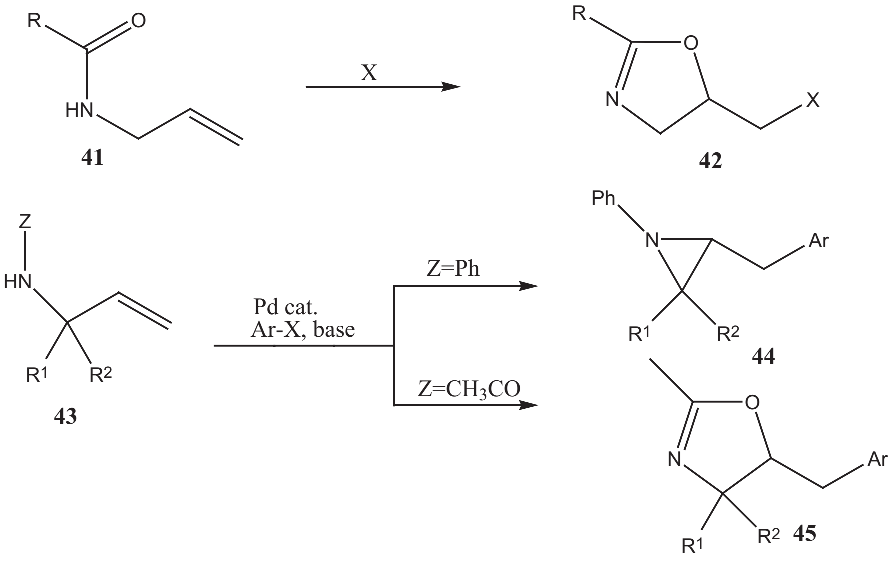
(Method IV): The phosphonic diamide prodrugs of the oxazole phosphonate FBPase inhibitor **39** were prepared using the dichloridate method [78].



Reagents and conditions: i. SO_2Cl_2; ii. amine, Hunig's base, CH_2Cl_2

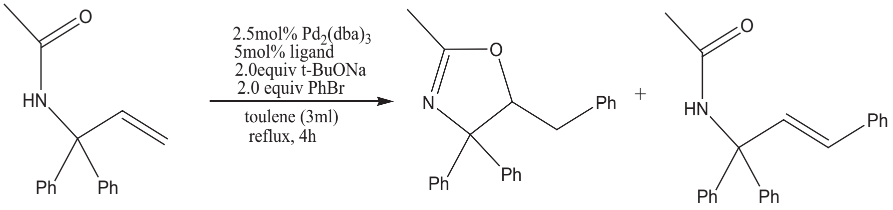
Scheme 12.8

Palladium-catalysed reactions of allylamine derivatives with aryl halides: Palladium-catalysed intramolecular arylative cyclisation reactions of *N*-Allylanilines with aryl halides to yield aziridines **44** (Z = Ph) and a similar reaction of *N*-Allylacetamides resulted in the selective formation of 5-benzyl-substituted oxazolines **45** without contamination by the corresponding aziridines **44** (Z = CH_3CO) [79–82] (Scheme 12.9).



Scheme 12.9

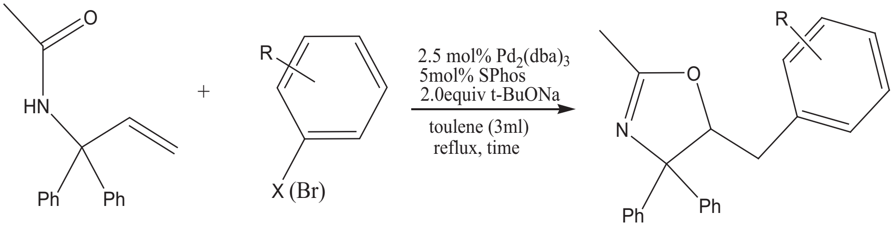
Effect of ligands on palladium-catalysed phenylative cyclisation reaction and competitive Mizoroki–Heck reaction: Palladium-catalysed intramolecular arylative cyclisation reactions of *N*-Allylacetamide **46** with bromobenzene afforded benzyl-substituted oxazoline **47** in 75 % yield. The cyclisation reaction inevitably competed with the Mizoroki–Heck reaction, which yielded **48** as the only identifiable by-product. Several ligands were screened, and bulky ligands are generally effective for the cyclisation (Scheme 12.10).



46 (0.30mmol) **47** **48**

Scheme 12.10

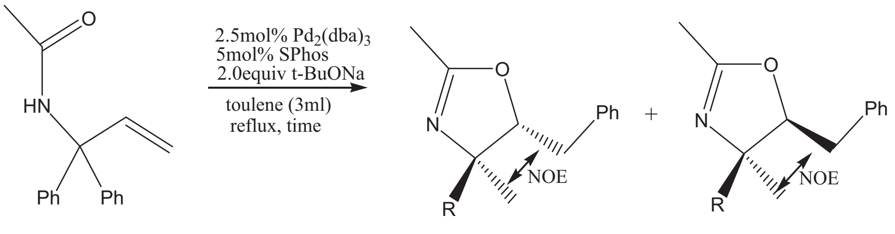
Scope of aryl halides: Aryl chlorides as well as aryl bromides participated in the reaction. Sterically demanding aryl bromides reacted smoothly. Electron-deficient fluorinated aryl bromides were also reactive. Aryl halides bearing a t-butoxycarbonyl, diethylaminocarbonyl or a cyano group underwent the arylative cyclisation to yield the corresponding products in good yields. The reaction of **46** with electron-rich 4-bromoanisole **49** resulted in a modest yield of **50** and formation of a significant amount of Mizoroki–Heck by-product (Scheme 12.11).



46 (0.30mmol) **49** 1.2(equiv) **50**

Scheme 12.11

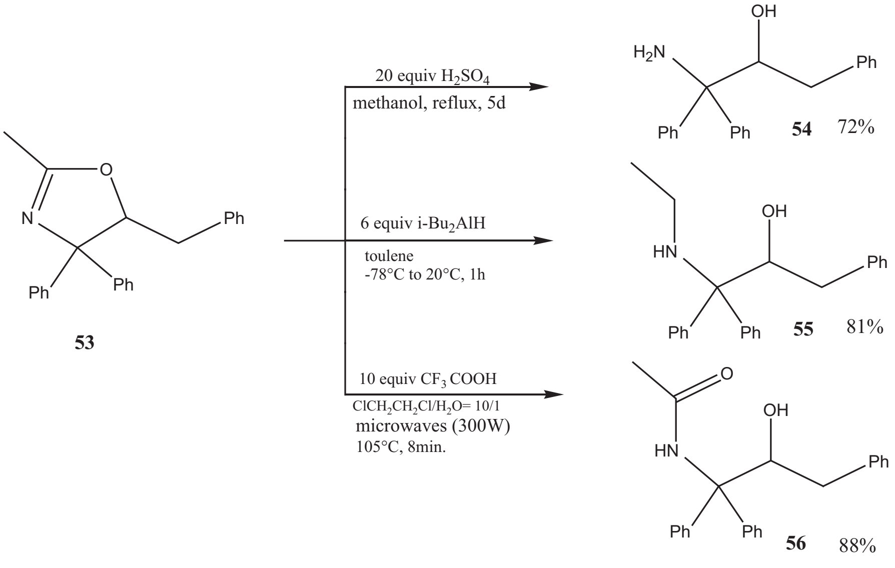
Diastereoselective cyclisation: *N*-Allylacetamides **46** that bear a stereogenic centre at the allylic position were prepared and subjected to the arylative cyclisation reaction. The reactions proceeded smoothly with good diastereoselectivity. The major isomers have the larger R group and the newly formed benzyl group is in a *trans* relationship. The relative stereochemistries of **51** and **52** were determined by NOE analysis (Scheme 12.12).



46 (0.30mmol) **51** (major) **52** (minor)

Scheme 12.12

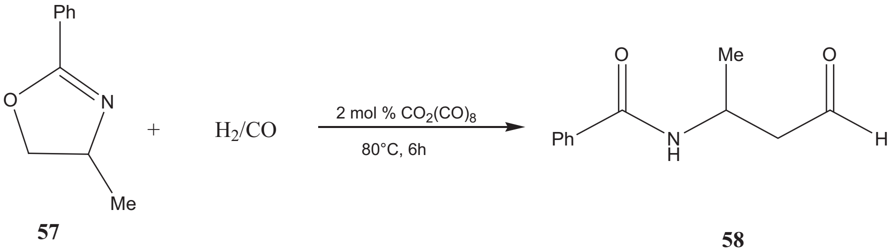
Transformation of oxazoline: 53 formed the amino alcohol derivatives **54** on opening of the ring with H_2SO_4. Reduction of **53** with diisobutylaluminium hydride provided *N*-Ethyl amino alcohol **55**. Oxazoline was converted to acetamide **56** by acidic hydrolysis with trifluoroacetic acid. The overall transformation of **53** to **56** represents the regioselective carbohydroxylation of *N*-Allylacetamide [83–84] (Scheme 12.13).



Transformation of oxazoline

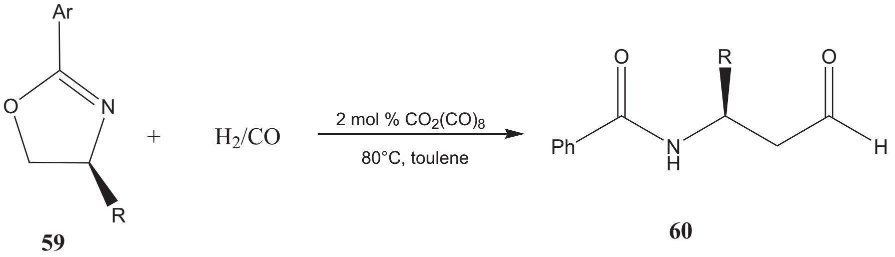
Scheme 12.13

Solvent effect on oxazoline hydroformylation: Solvent choice is important for achieving optimal rates and product selectivities in epoxide carbonylation and began by screening the hydroformylation of 4-methyl-2-phenyloxazoline in solvents of varying polarity and donicity. Solvents of moderate donicity such as tetrahydrofuran, diethyl ether and 1,4-dioxane also provided only modest yields of the desired product, while the strongly coordinating solvent acetonitrile completely inhibited the reaction; of the solvents screened, toluene proved to be the highest yielding (Scheme 12.14).



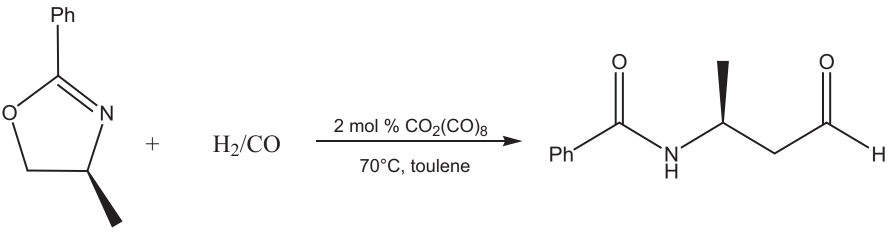
Scheme 12.14

Hydroformylation of oxazolines to β-amidoaldehydes: Oxazoline **59** undergoes carbonylation to form oxazinones which under the pressure of hydrogen and carbon monoxide gives a complicated mixture of products and only a small amount of the desired β-amidoaldehyde **60** (Scheme 12.15).



Scheme 12.15

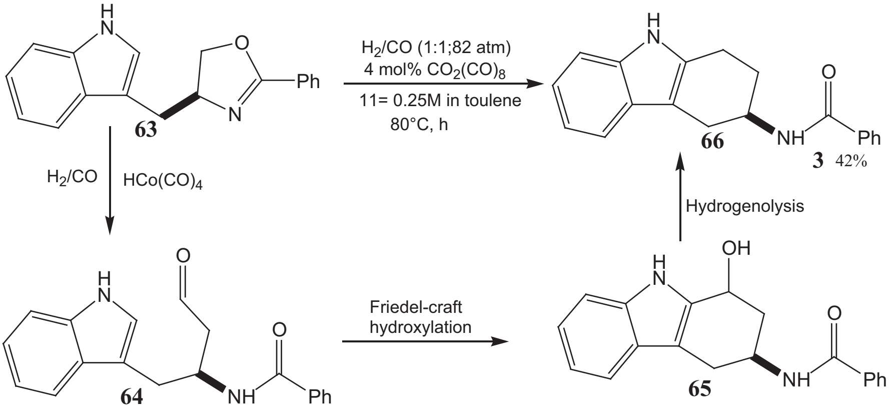
Effect of temperature on the hydroformylation of oxazoline: Oxazoline hydroformylation is also impacted by temperature and pressure. As the reaction temperature is lowered, an increase in the enantiomeric excess of β-amidoaldehyde **62** was observed. Also, an increase in % ee was observed when the total pressure of H_2/CO was increased. Hydroformylation at temperatures below 70°C led to the formation of significant amounts of oxazinone (Scheme 12.16).



61 **62**

Scheme 12.16

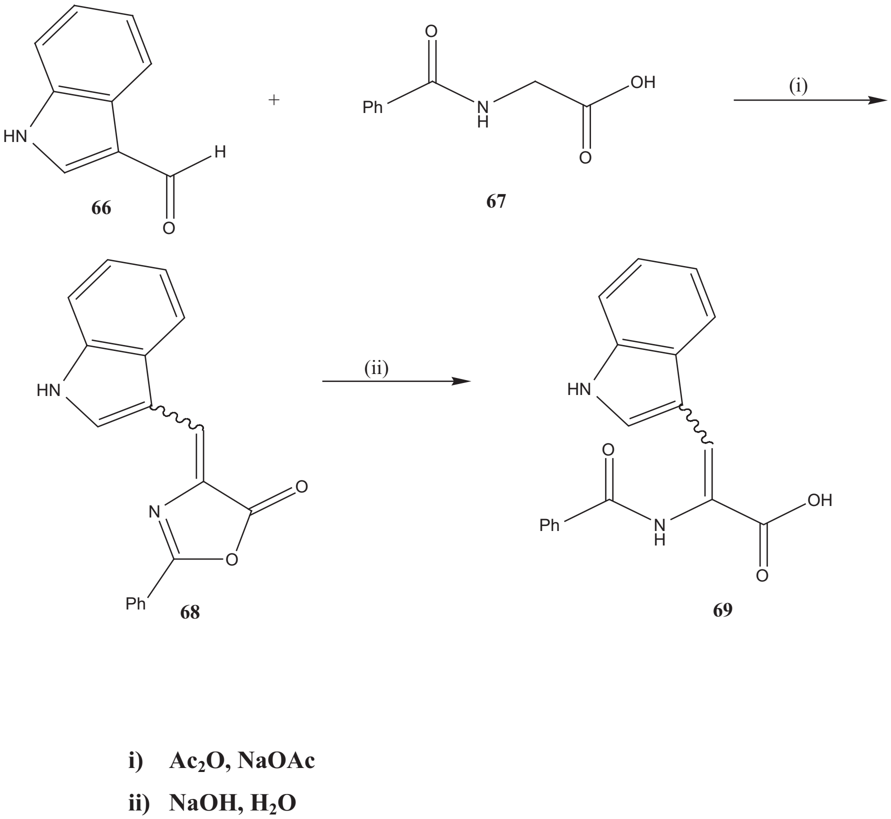
Hydroformylation: Hydroformylation of the tryptophan-derived oxazoline **63** led to the formation of tetrahydrocarbazole product **66**. In the reaction pathway, β-amidoaldehyde product **64** is initially formed, which is followed by intramolecular Friedel–Crafts hydroxyalkylation to give **65** (Scheme 12.17).



Scheme 12.17

3.1.3 Indole

Synthesis of dehydrotryptophan: The amino acid tryptophan was first synthesised by Erlenmeyer's method via the dehydrotryptophan intermediate. Ellinger et al. reacted indole-3-carbaldehyde **66** with the glycine derivative hippuric acid **67**, after which hydrolysis of the azlactone intermediate **68** afforded the dehydrotryptophan intermediate **69** [85] (Scheme 12.18).

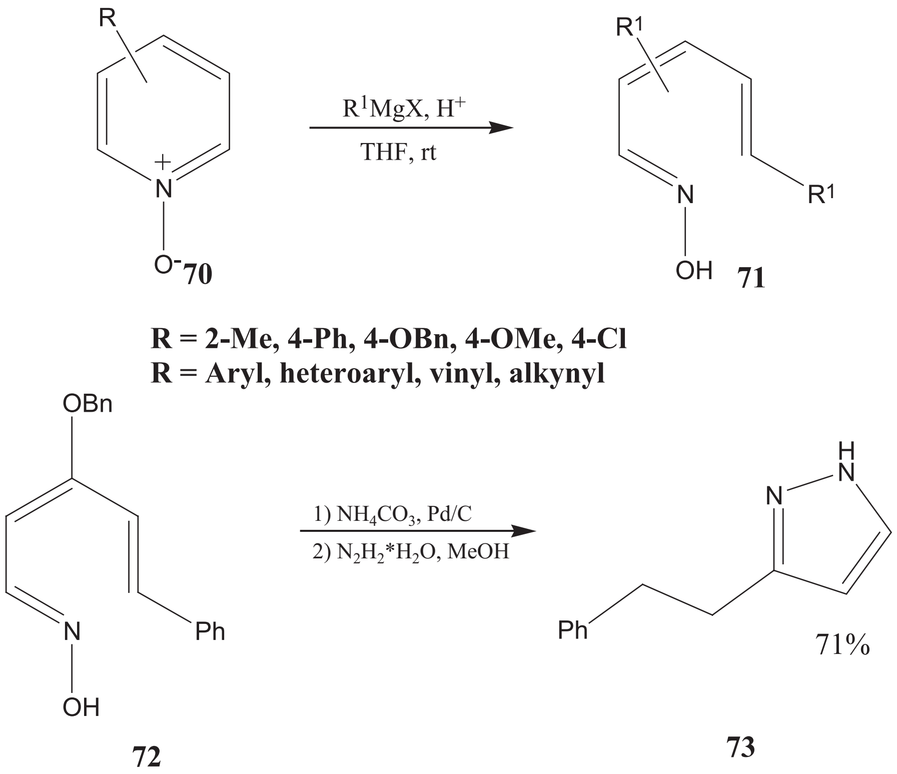


Scheme 12.18

(i) Ac_2O, NaOAc
(ii) NaOH, H_2O

3.1.4 Pyrazole

Synthesis of different substituted dienal-oximes and pyrazole: Addition of an activating group (e.g., chlorine, methoxy, etc.) at the 2 position of pyridine *N*-oxide **70** gives a diverse set of functionalized dienal-oximes **71**, which were used as starting materials in the synthesis of conjugated nitriles, aliphatic primary and secondary amines, enaminones and the substituted pyrazole **73** [86–88] (Scheme 12.19).



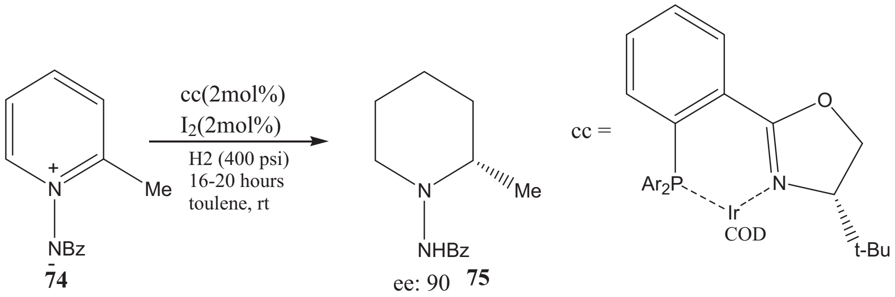
Scheme 12.19

3.2 *Synthesis of Six-Membered Heterocycles*

3.2.1 Piperidines

Piperidine is a widely used building block and chemical reagent in the synthesis of organic compounds, including pharmaceuticals.

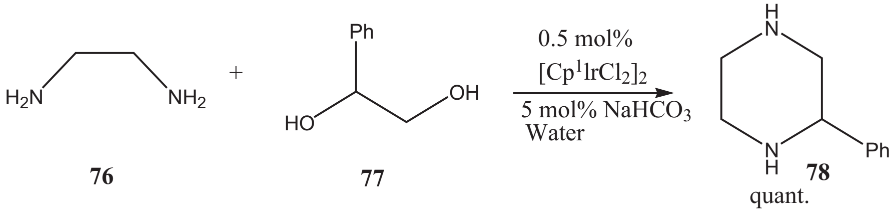
Synthesis of substituted piperidines: Charette and co-workers recently reported a method for the preparation of substituted piperidines from activated pyridines. The method is based on an iridium-catalysed asymmetric hydrogenation of *N*-Iminopyridinium ylides **74** for the synthesis of enantiomerically enriched piperidines **75** [89] (Scheme 12.20).



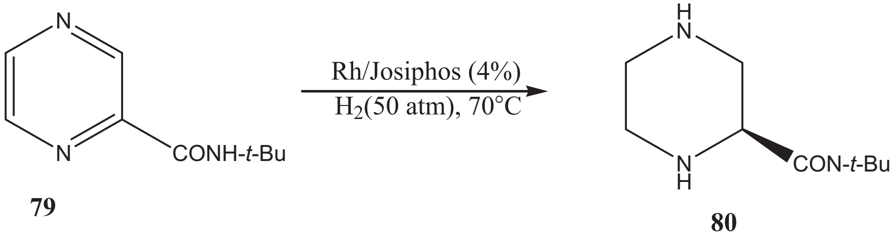
Scheme 12.20

3.2.2 Piperazines

Synthesis of piperazines: Madsen and co-workers recently reported an iridium-catalysed synthesis of piperazines from diamines **76** and diols **77**. Another procedure is the hydrogenation of pyrazines which gives piperazine [90–91] (Scheme 12.21).

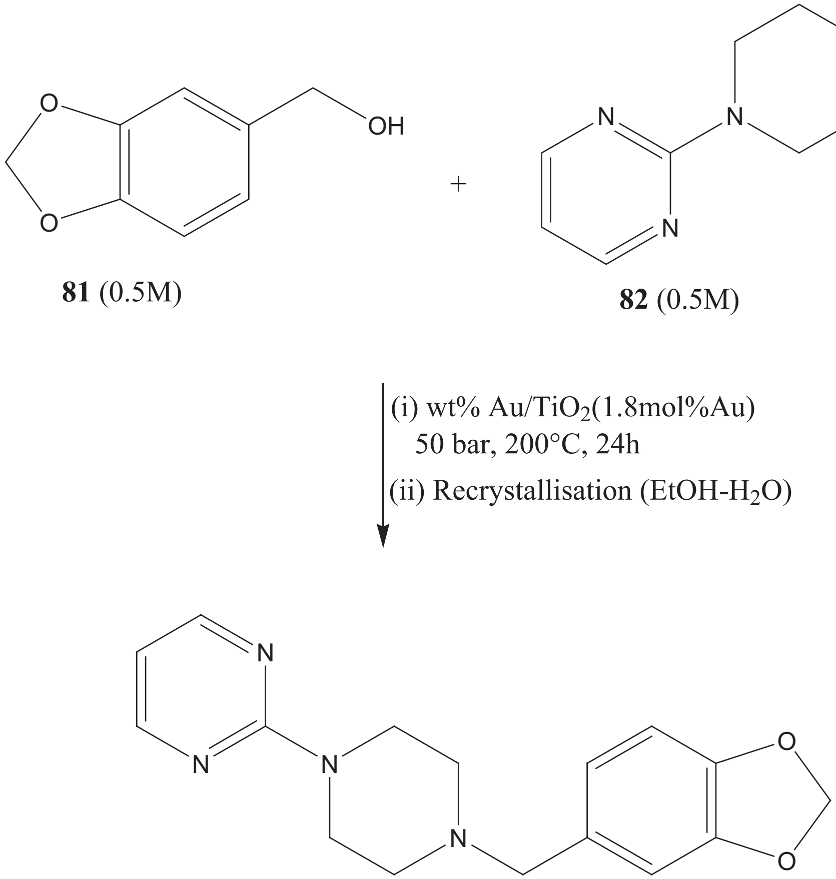


Another procedure is the hydrogenation of pyrazines **79** which gives piperazine **80**.



Scheme 12.21

Synthesis of piribedil: Direct alkylation of piperazine-substituted pyrimidine derivative **82** and benzyl alcohol derivative **81** in a 2:1 ratio gives piribedil **83** (Scheme 12.22).


OH
O
O
+
N
N
N
NH
(i) wt% Au/TiO$_2$(1.8mol%Au)
50 bar, 200°C, 24h
(ii) Recrystallisation (EtOH-H$_2$O)
N
N
N
N
O
O

81 (0.5M)

82 (0.5M)

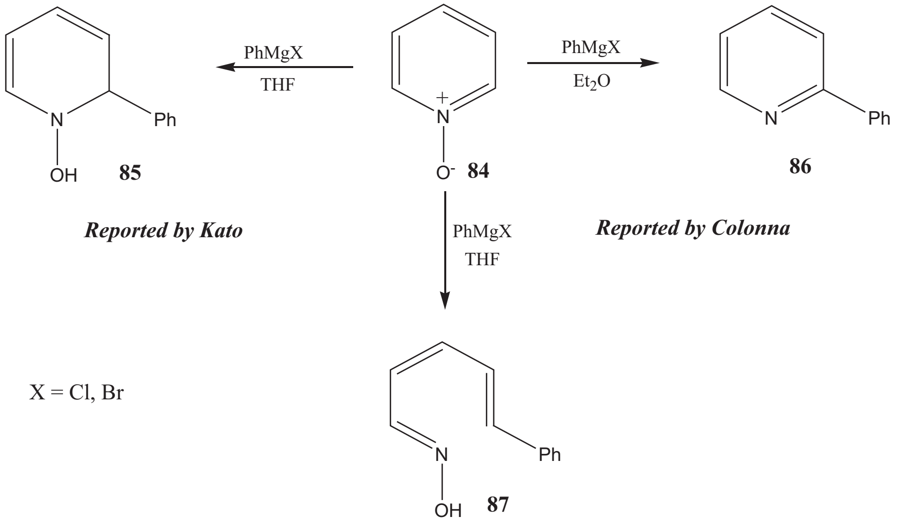
83, 77% (79% conversion)

Scheme 12.22

3.2.3 Pyridine

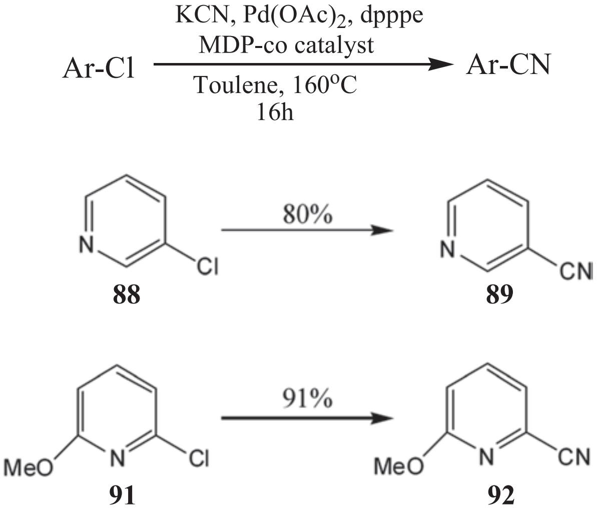
Pyridine has a conjugated system of six π-electrons that are delocalized over the ring. The molecule is planar and, thus, follows the Hückel criteria for aromatic systems.

Grignard additions to pyridine N-oxides: Colonna and co-workers published the first report on the reaction between Grignard reagents and pyridine *N*-oxide **84**. They isolated 1,2-dihydropyridine **85** in 60–80 % yield. The ring-opened dienal-oxime **87** was isolated in a low 28 % yield (Scheme 12.23).



Scheme 12.23

MDP-catalysed cyanation: Heteroaryl substrates converted to their corresponding nitriles under MDP (1–1′-methylenediperidine)-catalysed cyanation with best yields, such as **89** and **92** form **88** and **91**, respectively (Scheme 12.24).



Scheme 12.24

Acknowledgment We are grateful to the Department of Chemistry, Banasthali University, Banasthali and Department of Chemistry, FASC, Mody University of Science and Technology, Lakshmangarh, for providing the necessary facilities.

References

1. Clark JH, Luque R, Matharu AS (2012) Green chemistry, biofuels, and biorefinery. Annu Rev Chem Biomol Eng 3:183–207. doi:10.1146/annurev-chembioeng-062011-081014
2. Linthorst JA (2010) An overview: origins and development of green chemistry. Found Chem 12(1):55–68
3. Baron M (2012) Towards a greener pharmacy by more eco-design. Waste and Biomass Valorization 3:395–407. doi:10.1007/s12649-012-9146-2
4. Richard KH, Concepción JG, Constable DJC, Sarah RA, Graham GAI, Gail F, James S, Steve PB, Alan DC (2011). Expanding GSK's solvent selection guide—embedding sustainability into solvent selection starting at medicinal chemistry. Green Chem 13:854–862. doi:10.1039/C0GC00918K
5. Kumar A, Gupta G, Srivastava S (2011) Functional ionic liquid mediated synthesis (FILMS) of dihydrothiophenes and tacrine. Green Chem 13:2459. doi:10.1039/C1GC15410A
6. Eissen M, Metzger JO (2002) Environmental performance metrics for daily use in synthetic chemistry. Chem Eur J 8(16):3580–3585. doi:10.1002/1521-3765(20020816)8:16<3580
7. Centi G, Perathoner S (2003) Catalysis and sustainable (green) chemistry. Catal Today 77(4):287–297. doi:10.1016/S0926-3373(01)00286-7
8. Wender PA, Handy ST, Wright DL (1997) Towards the ideal synthesis. Chem Ind 19:765–769
9. Hudlicky T, Natchus MG (1993) in Organic Synthesis: Theory and Applications (Ed.: T. Hudlicky), Jai Press, Greenwich, CT
10. Wender PA (1996) Frontiers in organic synthesis: introduction. Chem Rev 96:1–2. doi:10.1021/cr950065y
11. Moseley JD, Kappe CO (2011) A critical assessment of the greenness and energy efficiency of microwave assisted organic synthesis. Green Chem 13:794–806. doi:10.1039/c0gc00823k
12. Bazureau JP, Paquin L, Carrié D, L'Helgoual'ch JM, Guihéneuf S, Coulibaly KW, Burgy G, Komaty S, Limanton E (2012) Microwaves in Heterocyclic Chemistry, in Microwaves in Organic Synthesis, Volume 1, Third Edition (eds A. de la Hoz and A. Loupy), Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany. doi:10.1002/9783527651313.ch16
13. Kumar A, Tripathi VD, Kumar P (2011) β-Cyclodextrincatalysed synthesis of tryptanthrin in water. Green Chem 13:51–54. doi:10.1039/c2gc36276g
14. Biermann U, Bornscheuer U, Meier MAR, Metzger JO, Schäfer HJ (2011) Oils and fats as renewable raw materials in chemist. Angew Chem Int 50:3854–3871. doi:10.1002/anie.201002767
15. Crabtree RH (2011) An organometallic future in green and energy chemistry. Organometallic 30(1):17–19. doi:10.1021/om1009439
16. Foley P, Crmanashahi PA, Beach ES, Zimmerman JB (2012) Derivation and synthesis of renewable surfactants. Chem Soc Rev 41:1499–1518. doi:10.1039/C2CS90006H
17. Mendu P, Pragathi J, Gyana KC (2011) Synthesis, spectral characterization, molecular modeling and biological activity of first row transition metal complexes with Schiff base ligand derived from chromone-3-carbaldehyde and o-amino benzoic acid. J Chem Pharm Res 3(4):602–613. ISSN No:0975–7384
18. Vrdoljak V, Dilovic L, Rubcic M, Pavelic SK, Kralj M, Matkovic CD, Piantanida I, Novak P, Rozman A, Cindric M (2010) Synthesis and characterisation of thiosemicarbazonatomolybdenum (VI) complexes and their in vitro antitumor activity. Eur J Med Chem 45:38–48

19. Sakthilatha D, Rajavel R (2013) The template synthesis, spectral and antibacterial investigation of new N2O2donor Schiff base Cu(II), Ni(II), Co(II), Mn (II) and VO(IV) complexes derived from 2-Hydroxy acetophenone with 4-chloro-2,6-diaminopyrimidine. J Chem Pharm Res 5(1):57–63
20. Adnan D (2013) Synthesis and characterization of Schiff bases derived from acetylacetone and their theoretical study. Int J Chem Tech Res 5:204–211
21. Wilbon PA, Chu F, Tang C (2013) Progress in renewable polymers from natural terpenes, terpenoids, and rosin. Macromol Rapid Commun 8:34–37. doi:10.1002/marc.201200513
22. Raynaud J, Wu JY, Ritter T (2012) Iron-catalyzed polymerization of isoprene and other 1,3-dienes. Angew Chem Int 51:11805–11808. doi:10.1002/anie.201205152
23. Zhang J, Matta ME, Hillmyer MA (2012) Hillmyer, synthesis of sequence-specific vinyl copolymers by regioselective ROMP of multiply substituted cyclooctenes. ACS Macro Lett 1(12):1383–1987. doi:10.1021/mz300535r
24. Baghbanzadeh M, Pilger C, Kappe CO (2011) Rapid nickel-catalyzed suzuki-miyaura cross-couplings of aryl carbamates and sulfamates utilizing microwave heating. J Org Chem 76(5):1507–1510. doi:10.1021/jo1024464
25. Beach ES, Weaks BR, Stern R, Anastas PT (2013) Plastic additives and green chemistry. Pure Appl Chem 85(8):1611–1624
26. Horton DA, Bourne GT, Smythe ML (2003) The combinatorial synthesis of bicyclic privileged structures or privileged substructures. Chem Rev 103:893–930. doi:10.1021/cr020033s
27. Vieth M, Siegel MGR, Watson EIA, Robertson DH, Savin KA, Durst GL, Hipskind PA (2004) Characteristic physical properties and structural fragments of marketed oral drugs. J Med Chem 47:224–232. doi:10.1021/jm030267j
28. Welsch MES, Snyder A, Stockwell BR (2010) Privileged scaffolds for library design and drug discovery. Curr Opin Chem Biol 14:347–361. doi:10.1016/j.cbpa.2010.02.018
29. Buffat MGP (2004) Synthesis of piperidines. Tetrahedron 60:1701–1729. doi:10.1016/j.tet.2003.11.043
30. Laschat S, Dickner T (2000) Stereoselective synthesis of piperidines. Synthesis 13:1781–1813. doi:10.1055/s-2000-8218
31. Abass M (2005) Fused quinolines. Recent synthetic approaches to azoloquinolines-a review. Heterocycles 65:901–965. doi:10.3987/REV-04-592
32. Henry GD (2004) For a thorough review of the history, applications and synthesis of pyridine derivatives. Tetrahedron 60:6043–6061. doi:10.1016/j.tet.2004.04.043
33. Nordstrom LU, Madsen R (2007) Iridium catalysed synthesis of piperazines from diols. Chem Commun 2007:5034–5036. doi:10.1039/B712685A
34. Undheim K, Efskind J (2000) Ru(II)-catalyzed ring closing metathesis in stereoselective spiroannulations and cascade reactions of cyclic dipeptide substrates. Tetrahedron 56:4847–4857. doi:10.1016/S0040-4020(00)00200-3
35. Brosse N, ElHage R, Chaouch M, P´etrissans M, Dumarcay S, G´erardin P (2010) Investigation of the chemical modifications of beech wood lignin during heat treatment. Polym Degrad Stab 95:1721–1726. doi:10.1016/j.polymdegradstab.2010.05.018
36. Ben H, Ragauskas AJ (2011) Heteronuclear single-quantum correlation-nuclear magnetic resonance (hsqc-nmr) fingerprint analysis of pyrolysis oils. Energy Fuels 25:2322–2332. doi:10.1021/ef2001162
37. Zawadzki J, Wisniewski M (2002) ^{13}C NMR study of cellulose thermal treatment. J Anal App Pyrolysis 62:111–121. (http://dx.doi.org/10.1016/S0165-2370(00)00217-5)
38. Ahmad T, Andersson R, Olsson K, Theander O (1993) On the formation of 2,3-dihydroxyacetophenone from pentoses or hexuronic acids. Carbohydr Res 247:211–215. doi:10.1016/0008-6215(93)84253-3
39. Luijkx GCA, Rantwijk FV, Bekkum VH (1993) Hydrothermal formation of 1,2,4-benzenetriol from 5-hydroxymethyl-2-furaldehyde and D-fructose. Carbohydr Res 242:131–139. (http://dx.doi.org/10.1016/0008-6215(93)80027-C)

40. Krishana R, Kallury MR, Ambidge C, Tidwell TT, Boocock DGB, Foster AA, Stewart DJ (1986) Rapid hydrothermolysis of cellulose and related carbohydrate. Carbohydr Res 158:253–261. doi:10.1016/0008-6215(86)84024-1
41. Shen DK, Gu S (2009) The mechanism for thermal decomposition of cellulose and its main products. Bioresour Technol 100:6496–6504. doi:10.1016/j.biortech.2009.06.095
42. Jakab E, Liu K, Meuzelaar HLC (1997) Thermal decomposition of wood and cellulose in the presence of solvent vapours. Ind Eng Chem Res 36:2087–2095
43. Tao F, Song H, Chou L (2011) Catalytic conversion of cellulose to chemicals in ionic liquid. Carbohydr Res 346:58–63. doi:10.1016/j.carres.2010.10.022
44. Tao F, Song H, Chou L (2010) Hydrolysis of cellulose by using catalytic amounts of $FeCl_2$ in Ionic liquids. ChemSusChem 3:1298–1303. doi:10.1002/cssc.201000184
45. Huang J, Liu C, Wei S, Huang X, Li H (2010) Density functional theory studies on pyrolysis mechanism of β-d-glucopyranose. J Mol Struct Theochem 958:64–70. doi:10.1016/j.theochem.2010.07.030
46. Hollmann F, Arends IWCE, Buhler K, Schallmey A, Buhler B (2011) Enzyme-mediated oxidations for the chemist. Green Chem 13:226–265. doi:10.1039/C1GC15424A
47. Hollmann F, Arends IWCE, Holtmann D (2011) Enzymatic reductions for the chemist. Green Chem 13:2285–2314. doi:10.1039/C1GC15424A
48. Dom´ınguez deMP, Stillger T, Pohl M, Kiesel M, Liese A, Gr¨oger H, Trauthwein H (2008) Enantioselective C-C bond ligation using recombinant E. coli whole cell biocatalysts. Adv Synth Catal 350:165–173. doi:10.1002/adsc.200700230
49. Jakoblinnert A, Mladenov R, Paul A, Sibilla F, Schwaneberg U, Ansorge-Schumacher MB, Dom´ınguez deMP (2011) Asymmetric reduction of ketones with recombinant E. coli whole cells in neat substrates. Chem Commun 47:12230–12232. doi:10.1039/C1CC14097C
50. Davis SE, Houk LR, Tamargo EC, Datye AK, Davis RJ (2011) Oxidation of 5-Hydroxymethylfurfural over supported Pt, Pd and Au catalysts. Catal Today 160:55–60. doi:10.1016/j.cattod.2010.06.004
51. Zope BN, Hibbitts DD, Neurock M, Davis RJ (2010) Reactivity of the gold-water interface during selective oxidation catalysis. Science 330:74–78. doi:10.1126/science.1195055
52. Satterfield CN, Bonnell AH (1955) Interferences in the titanium sulfate method for hydrogen peroxide. Anal Chem 27:1174–1175. doi:10.1021/ac60103a042
53. Zope BN, Davis RJ (2009) Influence of reactor configuration on the selective oxidation of glycerol over Au/TiO_2. Top Catal 52:269–277. doi:10.1007/s11244-008-9163-3
54. Erkkil A, Majander I, Pihko PM (2007) Reviews on asymmetric iminium ion catalysis. Chem Rev 107:5416–5470. doi:10.1021/cr068388p
55. Westermann B, Ayaz M, Van Berkel SS (2010) Enantiodivergent organocascade reactions. Angew Chem 49:846–849. doi:10.1002/anie.200904638
56. Ahrendt KA, Borths CJ, MacMillan DWC (2000) New strategies for organic catalysis: the first highly enantioselective organocatalytic Diels-Alder reaction. J Am Chem Soc 122:4243–4244. doi:10.1021/ja000092s
57. Wilson RM, Jen WS, MacMillan DWC (2005) Enantioselective organocatalysed intramolecular Diels-Alder reaction. The asymmetric synthesis of solanapyrone. J Am Chem Soc 127:11616–11617. doi:10.1021/ja054008q
58. Jen WS, Wiener JJM, MacMillan DWC (2000) New srategies for organic synthesis. The first enantioselective organocatalytic 1, 3 dipolar cycloaddition. J Am Chem Soc 122:9874–9875. doi:10.1021/ja005517p
59. Austin JF, MacMillan DWC (2002) Enantioselective organocatalytic indole alkylations. Design of a new and highly effective chiral amine for iminium catalysis. J Am Chem Soc 124:1172–1173. doi:10.1021/ja017255c
60. Lee S, MacMillan DWC (2007) Organocatalytic vinyl and friedel-crafts alkylations with trifluoroborate salts. J Am Chem Soc 129:15438–15439. doi:10.1021/ja0767480

61. Paras NA, MacMillan DWC (2002) Enantioselective organocatalytic 1,4-addition of electron-rich benzenes to α,β-unsaturated aldehydes. J Am Chem Soc 124:7894–7895. doi:10.1021/ja025981p
62. Chen YK, Yoshida M, MacMillan DWC (2006) Enantioselective organocatalytic amine conjugate addition. J Am Chem Soc 128:9328–9329. doi:10.1021/ja063267s
63. Gordillo R, Carter J, Houk KN (2004) Theoretical explorations of enantioselective alkylation reactions of pyrroles and indoles organocatalyzed by chiral imidazolidinones. Adv Synth Catal 346:1175–1185. doi:10.1002/adsc.200404107
64. Allemann C, Gordillo R, Clemente FR, Cheong PHY, Houk KN (2004) Theory of asymmetric organocatalysis of aldol and related reactions: rationalization and prediction. Acc Chem Res 37:558–569. doi:10.1021/ar0300524
65. Halland N, Hazell RG, Jørgensen KA (2002) Organocatalytic asymmetric conjugate addition of nitroalkanes to alpha, beta-unsaturated enones using novel imidazolidine catalysts. J Org Chem 67:8331–8338. doi:10.1021/jo0261449
66. Halland N, Aburel PS, Jørgensen KA (2003) Highly enantioselective organocatalytic conjugate addition of malonates to acyclic alpha, beta-unsaturated enones. Angew Chem 42:661–665. doi:10.1002/anie.200390182
67. Ouellet SG, Tuttle JB, MacMillan DWC (2004) Enantioselective organocatalytic hydride reduction. J Am Chem Soc 127:32–33. doi:10.1021/ja043834 g
68. Fischer O, Hepp E (1890) Ueber die fluorindine chem. Eur J Inorg Chem 23:2789–2793. doi:10.1002/cber.189002302190
69. Fischer O, Hepp E (1895) Ueber die fluorindine II. Eur J Inorg Chem 28:293–301. doi:10.1002/cber.18950280170
70. Wudl F, Koutentis PA, Weit A, Ma B, Strassner T, Houk KN, Khan SI (1999) Polyazaacenes: new tricks for old dogs. Pure Appl Chem 71:295–302. doi:10.1351/pac199971020295
71. Gao B, Wang M, Cheng Y, Wang L, Jing X, Wang F (2008) Pyrazine-containing acene-type molecular ribbons with up to 16 rectilinearly arranged fused aromatic rings. J Am Chem Soc 130:8297–8306. doi:10.1021/ja800311a
72. Kummer F, Zimmermann H (1967) Über die Elektronenspektren linearer Diaza-und Tetraaza-Acene. Ber Bunsenges Phys Chem 71(9–10):1119–1126. doi:10.1002/bbpc.19670710922
73. Seillan C, Brisset H, Siri O (2008) Efficient synthesis of substituted dihydrotetraazapentacenes. Org Lett 10:4013–4316. doi:10.1021/ol801509v
74. Miao S, Brombosz SM, Schleyer PR, Wu JI, Barlow S, Marder SR, Hardcastle KI, Bunz UHF (2008) Are N, N-Dihydrodiazatetracene derivatives antiaromatic? J Am Chem Soc 130:7339–7344. doi:10.1021/ja077614p
75. Wu JI, Wannere CS, Mo Y, Schleyer PR, Bunz UHF (2009) 4n p electrons but stable: N, N-dihydrodiazapentacenes. J Org Chem 74:4343–4349. doi:10.1021/jo900684c
76. Dang Q, Liu Y, Cashion DK, Kasibhatla SR, Jiang T, Taplin F, Jacintho J, Li H, Sun Z, Fan K, DaRe J, Tian F, Li W, Gibson T, Lemus R, Poelje VPD, Potter SC, Erion MD (2011) Discovery of a series of phosphonic acid-containing thiazoles and orally bioavailable diamide prodrugs that lower glucose in diabetic animals through inhibition of fructose-1,6-bisphosphatase. J Med Chem 54:153–165. doi:10.1021/jm101035x
77. Dang Q, Kasibhatla SR, Jiang T, Fan K, Liu Y, Taplin F, Schulz W, Cashion DK, Reddy KR, Poelje VPD, Fujitaki JM, Potter SC, Erion MD (2008) Discovery of phosphonic diamide prodrugs and their use for the oral delivery of a series of fructose 1,6-bisphosphatase inhibitors. J Med Chem 51:4331–4339. doi:10.1021/jm8001235
78. Sundermeier M, Zapf A, Mutyala S, Baumann W, Sans J, Weissand S, Beller M (2003) Progress in the palladium-catalyzed cyanation of aryl chlorides. Chem Eur J 9:1828–1936. doi:10.1002/chem.200390210
79. Hayashi S, Yorimitsu H, Oshima K (2009) Synthesis of aziridines by palladium-catalyzed reactions of allylamines with aryl and alkenyl halides: evidence of a syn-carboamination pathway. Angew Chem 48:7224–7226. doi:10.1002/anie.200903178

80. Lee KY, Kim YH, Park MS, Oh CY, Ham WH (1999) Stereoselective intramolecular cyclization of allyl and homoallyl benzamide via π-allylpalladium complex catalyzed by Pd(0). J Org Chem 64:9450–9458. doi:10.1021/jo991065r
81. Cook GR, Shanker PS (1998) Palladium-catalyzed formation and stereoselective isomerization of 5-vinyloxazolines. Tetrahedron Lett 39:3405–3408. doi:10.1016/S0040-4039(98)00534-6
82. Cookand GR, Xu W (2006) Palladium-catalysed addition of aryl iodides to N-(2,3-butadienyl)-benzamide followed by cyclisation was reported to afford 5-vinyloxazolines via p-allylpalladium intermediates. Heterocycles 67:215–232. doi:10.1021/ol052802a
83. Braun M, Fleischer R, Mai B, Schneider MA, Lachenicht S (2004) The regioisomeric triphenylaminoethanols-comparison of their efficiency in enantioselective catalysis. Adv Synth Catal 346:474–482. doi:10.1002/adsc.200303178
84. Benfatti F, Cardillo G, Gentilucci L, Tolomelli A, Monari M, Piccinelli F (2007) A microwave-enhanced, Lewis acid-catalyzed synthesis of 1,3-dioxolanes and oxazolines from epoxides. Adv Synth Catal 349:1256–1264. doi:10.1002/adsc.200600516
85. Block RJ (1946) The isolation and synthesis of the naturally accouring α-amino acids. Chem Rev 38:501–571
86. Youssif S (2001) Recent trends in the chemistry of pyridine N-oxides. Arkivoc 2:242–268. ISSN:1424–6376
87. Campeau LC, Stuart DR, Leclerc JP, Bertrand-Laperle ME, Villemure HY, Sun S, Lasserre N, Guimond M, Lecavallier Fagnou K (2009) Palladium-catalyzed direct arylation of azine and azole N-oxides: reaction development, scope, and applications in synthesis. J Am Chem Soc 131:3291–3306. doi:10.1021/ja808332k
88. Coperet CH, Adolfsson TA, Khuong V, Yudin AK, Sharpless KB (1998) A simple and efficient method for the preparation of pyridine-N-oxides II. J Org Chem 63:1740–1741. doi:10.1021/jo9723467
89. Legault CY, Charette AB (2005) Catalytic asymmetric hydrogenation of n-iminopyridinium ylides: expedient approach to enantioenriched substituted piperidine derivatives. J Am Chem Soc 127:8966–8967. doi:10.1021/ja0525298
90. Zhou YG (2007) Asymmetric hydrogenation of heteroaromatic compounds. Acc Chem Res 40:1357–1366. doi:10.1021/ar700094b
91. Andersson H, Banchelin TS, Das L, Gustafsson S, Olsson MR, Almqvist F (2010) Complete regioselective addition of grignard reagents to pyrazine N-oxides, toward an efficient enantioselective synthesis of substituted piperazines. Org Lett 12:284–286. doi:10.1021/ol902619h